BROOKE'S BOOK

Despair to Hope: Disease Prevention Through Vaccines

By Mary Anne Jackson, MD, and Christopher Harrison, MD

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The photo on the cover page shows Brooke McGrath with her 3-year-old niece, Lydia McGrath. It was taken on January 8, 2011 (prior to Brooke's brother's wedding) about 60 hours before Brooke died. Lydia loved her Aunt Brookie and Aunt Brookie loved her niece Lydia. They had already developed a most special bond.

INTRODUCTION

From the Authors:

Childhood vaccinations are recognized as being among the most successful health-related advances of the last century. Children no longer die from polio, tetanus or diphtheria in the United States. Cases of the most common form of winter diarrhea (rotavirus), chickenpox and a previously common form of bacterial meningitis (*Haemophilus influenzae* type b) are almost unheard of now due the development and widespread use of specific vaccines. The United States vaccine schedule now allows us to protect children from 16 different diseases-including two that prevent cancers (hepatitis B and HPV vaccines).

Still, vaccine-preventable diseases continue to be a challenge. Some parents are opting out of vaccines and the resultant loss of herd immunity in some communities is responsible for outbreaks of diseases like whooping cough and measles. In many cases, those most severely affected are the youngest of children who are not yet eligible for vaccines.

Nevertheless, research continues to produce new vaccines to expand the number and type of infections that we can prevent. Other work strives to ensure that vaccines like polio vaccine can reach children worldwide. Diseases like tuberculosis and malaria cause millions of child deaths annually around the globe, and work is ongoing to develop vaccines that will prevent these infections.

This book tells the stories of individual children, teenagers, adults and families who experienced vaccine-preventable infections or other diseases that vaccines have not eliminated. The book celebrates successes of the past as we keep an eye on the future. It highlights potential successes that will be made possible from ongoing scientific discovery and innovation in the field of vaccine research, many of them happening right here at Children's Mercy Kansas City.

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AT A GLANCE: DISEASE PREVENTION

Pathogens/childhood infections 100 percent preventable by routine vaccination:

- Diphtheria
- Polio
- Congenital rubella syndrome (birth defects associated with rubella contracted by mother during pregnancy)
- Smallpox

Pathogens/childhood infections more than 99 percent preventable by routine vaccination:

- Measles
- Mumps
- Rubella
- *Haemophilus influenzae* type b (bloodstream infection and meningitis)

Pathogens/childhood infections more than 95 percent preventable by routine vaccination:

- Varicella (chickenpox)
- Rotavirus (winter childhood diarrhea)
- Tetanus
- Hepatitis A

Pathogens/childhood infections for which routine vaccination prevents substantial morbidity and mortality:

- Pertussis (whooping cough)
- Influenza (when vaccine strains match the circulating strains of seasonal influenza)
- *Neisseria meningiditis* serogroups A, C, Y, W (bloodstream infection and meningitis)
- *Streptococcus pneumoniae* (meningitis, bloodstream infection, pneumonia and acute otitis media)

Pathogens/infections for which routine vaccination can prevent cancer:

- Hepatitis B (prevents liver cancer)
- Human papillomavirus (prevents cervical, genital and other anal/oral cancers)

Recently available vaccines:

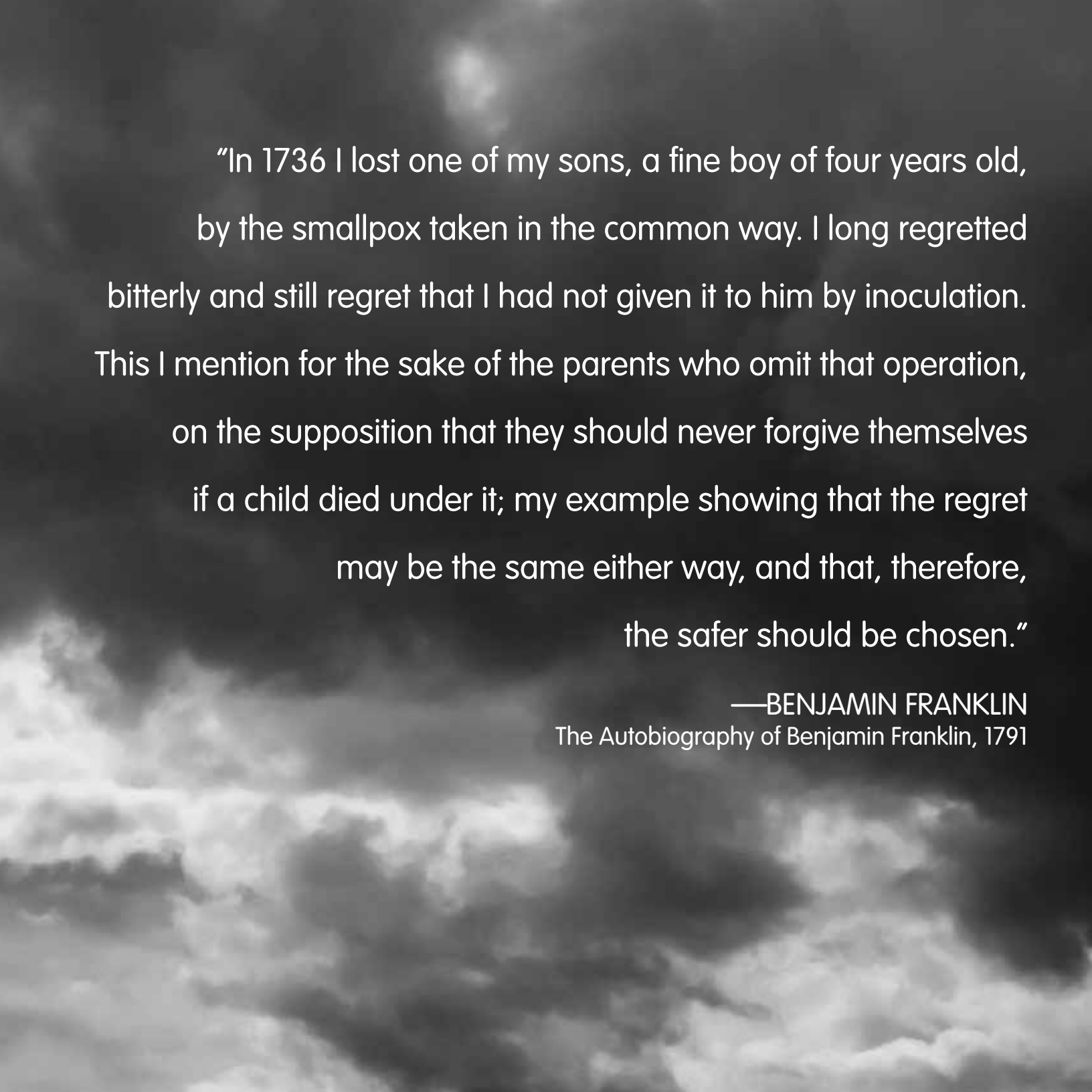
- Meningococcus serogroup B – for high-risk 10-25 year olds, but age eligibles soon to be expanded
- Human papillomavirus (covering additional five serotypes) – 9 valent (HPV9)

The current pediatric immunization schedule protects against 16 different types of infections. There are other vaccines that are eligible for older adults and travelers.

Most immunizations routinely recommended for children protect against infections by inducing the patient's own immune system to form antibodies.

Vaccines can be made from an attenuated or weakened form of a live bacteria or virus- and they do so by inducing an immune response that is very similar to that of natural infection. Live attenuated vaccines that are part of the routine pediatric vaccine schedule include measles, mumps, rubella, varicella, rotavirus and the nasal influenza vaccines. Because live attenuated vaccines rely on the patient's own immune system, they are not recommended in children who have any diseases (e.g., cancer) or who are being treated with certain medicines (e.g., corticosteroids) that impair the immune system.

Inactivated vaccines are made from viruses, bacteria or other protein-based components of a bacteria. Inactivated vaccines cannot replicate so they are safe for all children. The antibody titer can decrease over time so booster doses are needed. Inactivated vaccines include polio, hepatitis A, influenza (shot form), pertussis, hepatitis B, human papillomavirus, diphtheria and tetanus. Meningococcus, pneumococcus and Haemophilus influenzae type b vaccines are also inactivated vaccines made from a bacterial product that is attached to a protein (conjugated) to allow it to achieve better immunity for infants and children.



"In 1736 I lost one of my sons, a fine boy of four years old, by the smallpox taken in the common way. I long regretted bitterly and still regret that I had not given it to him by inoculation. This I mention for the sake of the parents who omit that operation, on the supposition that they should never forgive themselves if a child died under it; my example showing that the regret may be the same either way, and that, therefore, the safer should be chosen."

—BENJAMIN FRANKLIN
The Autobiography of Benjamin Franklin, 1791

TO CONQUER: PAST, PRESENT AND FUTURE

Childhood vaccinations have been recognized as the most important technological advances of the last century. No longer do children die from polio, tetanus or diphtheria in the United States. Still there are vaccine-preventable diseases that have challenged the public health community and some that on a global scope continue to result in millions of child deaths annually. This book will tell the story from the point of view of families impacted by vaccine-preventable infections, celebrating the successes of the past and underscoring the importance of continued scientific discovery and innovation.

The stories and related vaccine-preventable diseases featured in this book are categorized three ways: Conquered/Conquering, Nearly Conquered and Not Conquered:

Conquered/Conquering

- **Haemophilus influenzae type b** – This bacteria was the most common cause of spinal meningitis through 1993, when a conjugate vaccine was introduced into the routine infant vaccine schedule. Routinely tens of thousands of children were affected in the United States and those with meningitis were at risk for deafness (the most common sequelae), stroke and cognitive problems, not counting deaths in approximately 5 percent. Since the implementation of this highly effective and safe vaccine, more than 99 percent of cases have been prevented.
- **Chickenpox** – Previously thought of as a benign and inevitable disease of childhood, varicella affected 90 percent of children by their ninth birthday in the pre-vaccine era. In the late 1980s and early 1990s, there were outbreaks of streptococcal skin infection which complicated chickenpox (hailed by the media as "flesh-eating bacteria") which in some cases caused loss of limb and death. Varicella vaccine, which was licensed and implemented in 1995 in the United States has resulted in an 80 percent decrease in the burden of disease, with fewer hospitalized children and fewer deaths.

Nearly Conquered

- **Whooping cough** – Since the advent of vaccine, the U.S. burden of disease has gone from nearly a million cases a year to a few thousand. Not only do children under 6 months of age (too young to be protected by vaccine) have a greater chance of dying if they contract whooping cough, those that survive suffer a disease that lasts for months. Affected infants develop paroxysms of cough on average up to 30 times a day. These coughing episodes can be persistent with continuous coughing preventing the child's ability to take in a new breath for up to several minutes. This may cause the child to turn blue and stop breathing. Pneumonia and seizures may occur and deaths are most common in those under 3 months of age. While a safe and effective vaccine was available since the early 1960s, a suitable vaccine was not developed for older children and adults until 2009. This past year, nearly 10,000 were affected by an outbreak of whooping cough in California, and 10 infants died. A notable proportion of pertussis cases now are due to families choosing to not immunize their children.
- **Pneumococcus** – *Streptococcus pneumoniae* is the most important bacteria causing ear infections, pneumonia and meningitis in children. A conjugate vaccine that covered the seven most common serotypes wiped out 50 percent of cases. A newer vaccine which covers six new serotypes plus the seven in the first vaccine continues to reduce the morbidity and mortality from this bacterial infection.
- **Measles** – Measles remains a common disease in many parts of the world. In the United States, an effective vaccine is recommended for all children except those with some immune problems; however, measles cases imported into the United States in individuals who were not immunized have caused at least one large outbreak in 2015 and at least one death.

Not Conquered

Certain diseases are still a challenge because of the global scope of disease and/or the lack of an effective vaccine (until recently Meningococcus serogroup B).

- **Hepatitis B** – Global scope issue
- **Typhoid** – Global scope issue
- **Polio** – Pakistan and Afghanistan have had polio cases in 2015
- **Meningococcus serogroup B (MenB)** – Vaccines approved in 2015

DEDICATION

Brooke's Book is the result of trying to find a way to honor and remember our precious daughter and sister, Brooke Tivol McGrath. On January 11, 2011, Brooke died suddenly and unexpectedly at the age of 28 in New York City, where she lived and worked. *Neisseria meningitidis* serogroup B bacteria, a virulent and indiscriminate killer disease, took Brooke from us within hours of manifesting its symptoms.

On January 8, 2011, Brooke was in Kansas City celebrating her younger brother's wedding with family and friends, with no signs of sickness or ill health. Less than 58 hours later, Brooke was dead. As a family, we celebrated a joyful wedding on a Saturday night and then on the following Sunday (eight days later) we buried our precious daughter and sister.

During my search to find a way to honor and remember Brooke, I was placed in contact with Mary Anne Jackson, MD, Director of the Infectious Diseases Division at Children's Mercy. Dr. Jackson mentioned a book she wanted to do regarding the various meningococcal and meningococcemia bacteria, other meningitis-related bacteria, and various viruses, some for which successful vaccines have been developed and others for which vaccines have not yet been developed. The book would also discuss the research being conducted

regarding new varieties of these bacteria and viruses. There would be real-life stories of patients who were treated at Children's Mercy for these types of bacterial and viral infections and the impact on their families and friends. As a result of my conversations with Dr. Jackson and others at the hospital, *Brooke's Book* was developed and became a reality for Dr. Jackson and me. Although I would not be doing *Brooke's Book* in collaboration with Children's Mercy if Brooke had not died how she did, it is a meaningful and appropriate way in which to honor and remember Brooke.

Many of the cases involving *Neisseria meningitidis* serogroup B bacteria have the same tragic facts: a person experiences flu-like symptoms, and then 10 to 15 hours later dies. It is too emotionally difficult to understand and accept what happened and how unimaginably quickly it transpired, only a matter of hours from beginning to end. It is my hope that future losses like Brooke's can be avoided by greater awareness of certain infectious diseases. I also hope that *Brooke's Book* will increase the awareness of the research and development of vaccines needed to fight such diseases.

I love Brooke and miss her deeply every day. Brooke's passing changed the way I will live the rest of my life. Nothing prepared me for her death and its effect on my life. In trying to make some sense of this seemingly senseless tragedy, I wanted to do something in her honor and memory. I also believe that Brooke would want me to do something. If, because of *Brooke's Book*, one child is saved and his/her family and friends are spared the pain and heartbreak that a situation like this brings, it will honor Brooke's memory.

Brooke was always there for me as my daughter with her unconditional love and kindness and her helpful advice. Many of Brooke's friends made similar statements about Brooke's friendship and loyalty. We were each blessed to spend time on this earth with Brooke. We will forever be shaped by her beauty, grace and humor because Brooke's spirit lives on in each of us. I will always honor and remember Brooke by helping others in my life in the same way that Brooke helped me.

Brooke's Book may have started as a way to honor Brooke because of the manner in which she died, but my involvement with *Brooke's Book* led me to a different perspective. I dedicate *Brooke's Book* to my precious Brooke, not for how she died, but for how she lived.

Brooke's Dad,
Tom McGrath

BROOKE McGRATH

NEISSERIA MENINGITIDIS SEROGROUP B / NOT CONQUERED

As Brooke's Dad, as it would be for any parent who has lost a child, I struggled with how to write Brooke's story for this book, with how to share the story of your own child's death. I simply did not know how to put into words how we felt after deadly bacteria had so incredibly quickly taken Brooke from us. It was as if I was waiting for Brooke to inspire me or somehow inform me what to write. I do believe that Brooke did inspire and assist me with what I have ultimately written.

Brooke celebrated her 28th birthday on December 1, 2010, with several friends at a small New York City restaurant. She sent happy candid photos from the fun-filled evening to her Mom and me. Brooke was a vibrant, energetic and beautiful young woman. Life was good, busy and fulfilling. She was very close to her family and many friends, had her dream job in the jewelry industry in NYC, and loved her modest apartment in the West Village. Brooke's future appeared bright and further success inevitable.

Her brother, Hunter, was getting married in Kansas City on Saturday, January 8, 2011, and Brooke was one of the bridesmaids. Brooke came home to Kansas City on Thursday, January 6, to help with the last-minute preparations for the wedding. She enjoyed time with family before the wedding, including a very festive and celebratory pre-nuptial party on Friday night. Brooke was very active at the joyous family wedding. She danced with me many times and was an integral part of the hora, which was one of the highlights of the evening. After a fantastic weekend with family, Brooke returned to New York City on January 9.

On Monday morning, January 10, Brooke made a spirited and successful presentation to a client. In the afternoon Brooke began to feel tired and achy, experiencing mild flu-like symptoms, and left her office to rest at home. As the hours passed, the symptoms got progressively worse. Brooke contacted her Mom and kept us informed. Finally, Brooke called for an ambulance and arrived at the hospital Emergency Room around 12:45 a.m. on January 11. Brooke died at 5:40 a.m., less than five hours after arriving at the Emergency Room. In a matter of hours, Brooke went from a happy healthy young woman to dying from *Neisseria meningitidis* serogroup B bacteria causing a bloodstream infection.

The bacteria, *Neisseria meningitidis* (also known as meningococcus), is classified into 12 different serogroups worldwide. There are five serogroups that are most often seen in the United States. Serogroups B, C and Y each have traditionally accounted for approximately one-third of all cases reported in the United States. Vaccines have been available for serogroups A, C, W and Y for decades and recent recommendations for their use in preteens through young adults appear to be reducing disease due to W, Y and C.

Serogroup B has also been important, but is more in the public eye now for several reasons. Outside the United States, prolonged outbreaks of type B disease have been reported in New Zealand and France. It is also the serogroup which has for many decades caused 50-60 percent of infant cases in the United States. More recently in the United States, the prevalence of serogroup B disease has increased in young adults with outbreaks at universities on both United States coasts. But there is also good news. The FDA approved serogroup B vaccines in 2014 and they have recently gone into general use for high-risk patients in 2015.

Up to 10 percent of the population may carry the meningococcus germ in the nose. Even higher carriage rates may occur in adolescents and young adults. While acquiring meningococcus in the nasal area must occur before disease develops, only a minority of carriers ever develop symptoms. Typically, the bacteria is spread or transferred through the exchange of saliva or other respiratory secretions during activities like coughing, sneezing, chewing on shared items (chewing gum), kissing, or sharing food, water bottles or drinks.

Meningococcemia is the name given to bloodstream infections caused by *Neisseria meningitidis*. It often starts with mild nonspecific flu-like symptoms (which may include fatigue and achiness), but then progresses rapidly often with irreversible shock and organ failure. Death may occur within hours in as many as 40 percent of the cases, even if appropriate supportive and antibiotic therapy is given. Up to 20 percent of survivors have permanent injury. These injuries can involve brain damage from meningitis or gangrene-like injuries. The gangrenous processes can result in loss of limbs from the need to amputate one or several limbs, or shriveling and loss of body parts (e.g., ears or nose). This tissue damage usually starts on the first day of infection.

The severe tissue injury begins with a very distinctive skin rash. It begins as small bright red freckle-like spots that don't blanch when touched. These are known

as "petechiae." They usually expand into larger lesions called purpura fulminans (which looks like blackish-purple spots or patches on the skin). The purpura, which also has been described as "blossoming bruises," usually starts on legs or arms and can cover up to 25 percent of the body. The first sign of invasive meningococcal disease is often the petechiae shifting to purpura. Purpura is a sign of fulminant, serious and rapidly progressive disease.

Special risks for invasive or recurrent meningococcal disease include persons with certain types of immune problems. These include either lack of a part of the immune system, or not having a functioning spleen. Some people are born without spleens or have their spleens surgically removed for medical conditions. Others lose function of their spleens due to diseases such as sickle cell disease. Additional high-risk adolescents and adults include: college students living in residence halls, military recruits, being a microbiologist who is routinely exposed to *Neisseria meningitidis,* or travelers to or residents of countries in which meningococcal disease is common.

Outbreaks of disease are known to occur in closed populations such as in soldiers on military bases or college students living in college dormitories, e.g. the meningococcal B infections in colleges in 2014. That is why these groups have routinely been immunized against meningococcus A, C, W and Y serogroups. Now that meningococcal B vaccines are

approved for use in high-risk adolescents and adults, hopefully disease due to this serogroup B will diminish as much as it has for the other serogroups over the past decade. And hopefully the serogroup B vaccines will soon be approved for younger children who have traditionally been at highest risk for type B disease.

Although there was no vaccine available at the time for the deadly bacteria that invaded Brooke, as stated above there is now a vaccine that may be very helpful in fighting the disease. I certainly hope and pray that will be true very soon. I feel a very strong ongoing connection with Brooke. Her presence in my life remains most important to me and affects how I live my life. Zichrona livracha, may her memory be a blessing.

VACCINE UPDATE

As of the summer of 2015, the Advisory Committee on Immunization Practices (ACIP) made a category B recommendation that serogroup B meningococcal vaccine be given to adolescents and young adults from 16 through 23 years of age. Because this gives short-term protection against most strains of serogroup B meningococcus, the preferred age for administration seems to be 16 through 18 years of age. Administration any time during these three years should provide protection through the ages when people attend college and also the ages of highest prevalence of meningococcal disease.

Clinicians can utilize the FDA-approved two-dose series for the meningococcal serogroup B vaccine represented as MenB-4C, or the three-dose series of the alternative vaccine MenB-FHbp. Currently the ACIP recommendation is to maintain the same vaccine product for all doses of the series, with no overall preference for either product. Available data and prevailing expert opinion as of mid-2015 indicate that meningococcal group B vaccines can be given concurrently, but at a different anatomical site from other adolescent vaccines.

ELLIOTT BOREN
PNEUMOCOCCAL MENINGITIS / NEARLY CONQUERED

Amy Boren speaks with a calm, soft sadness about her son, Elliott. She shares the story of Elliott's death at seven months from pneumococcal meningitis, in hopes that other families can learn from her family's tragedy. Amy's insights grew from her experiences as a parent and from her career in pediatric nursing, and illuminate the painful reality that, even when parents do everything right, they can't always protect their children from contracting a horrible disease.

Born a full-term, healthy baby, Elliott was the second son in Amy and Jeff Boren's growing family. They followed suggested pediatric care guidelines, and Elliott received all of the recommended vaccinations during his first six months. When he was 7 months old, in December of 2007, Elliott developed fever and vomiting. Amy became worried when he seemed less active, so she took him in to an urgent care clinic where they diagnosed a stomach virus. She became increasingly concerned when Elliott seemed more lethargic and just three hours after the urgent care clinic visit, she took Elliott to the Mildred Lane Kemper Emergency Care Center at Children's Mercy Adele Hall Campus. There lab results confirmed that Elliott had a bacterial infection of the blood which led to meningitis (an infection of the fluid around the brain). The infection was confirmed to be caused by a bacterial germ called pneumococcus, also known as Streptococcus pneumoniae. Within 48 hours, despite the best antibiotics and intensive care, Elliott developed a devastating complication of his infection which resulted in kidney failure and destruction of red blood cells and those cells responsible for blood clotting. He was placed on the ventilator and started kidney dialysis. An MRI of his brain confirmed that the meningitis had resulted in multiple strokes. Elliott died three days after being admitted to the hospital.

Elliott received all routine childhood vaccines at the appropriate age, including a vaccine that protected against pneumococcal infection. This vaccine targeted the seven most common strains that cause infection in children, and was first introduced in October 2000. The success of the pneumococcal vaccine was unquestionable. After being included in the routine vaccine schedule for infants, doctors saw a greater than 75 percent reduction in childhood pneumococcal infections including pneumonia, bloodstream infections, meningitis and heart and skeletal infections. But investigators recognized that a better vaccine was still needed because there were still children like Elliott who were dying of pneumococcal infection. In February 2010, an improved formulation of pneumococcal vaccine was released which has already been shown to protect an even greater number of children.

Amy wonders if parents who avoid vaccinating their children have ever seen the full breadth of the damage these diseases can cause. "Parents who have chosen not to vaccinate their children just don't realize how important it is to take advantage of medical resources. They don't realize how lucky they are to have this opportunity for protection against serious diseases. Vaccines are the greatest medical advancement of my generation. Simply put, they save lives."

Amy encourages parents to trust the research and testing process that supports the regulation and formulation of new vaccines. If anything, she wonders, why don't we have more vaccines, with broader protection against diseases,

for our most vulnerable, our children? Amy devotes her days to taking care of her family and to taking care of other people's sick children, firmly hoping they will never have to experience the unfathomable loss that she and Jeff experienced. She suspects she will always wonder what else she could have done to protect her son from the horrific chain of events that claimed his life.

Bacterial Meningitis

Prior to 1990, the pathogens most commonly associated with bacterial meningitis in children over 3 months of age were Haemophilus influenzae type b and Streptococcus pneumoniae. Children under 5 years were most at risk and typically presented with high fever, headache, irritability, lethargy and seizures. Even when identified and treated early with appropriate antibiotics, 5 percent of children died from complications of the infection and 20 percent suffered long lasting effects, most commonly deafness. Substantial progress has been made in the last 25 years to eliminate bacterial meningitis in children. Disease dramatically declined following the introduction of the first Haemophilus influenzae type b (Hib) conjugate vaccines in the United States in 1990. Up to that time, Hib was the leading cause of bacterial meningitis and infants between 3 and 12 months of age were most commonly affected. The virtual elimination of Hib meningitis is regarded to be one of the most impressive vaccine success stories ever. By the year 2000, a 99 percent reduction in disease was noted with the few cases now seen usually occurring in unimmunized children or in those too young to be immunized.

Because there are more than 90 serotypes of pneumococcus, vaccines were developed and targeted to those strains most commonly associated with severe infection in children. The vaccines developed and introduced into the childhood vaccine schedule in 2000 were focused on protection against seven strains of pneumococcus. Newer conjugate vaccines which protect against 13 of the possible strains, associated with severe infection in children, were implemented in 2010. By 2010, an 88 percent reduction in all types of pneumococcal invasive infection in children under 5 years of age was reported. The 13-valent vaccine is given at 2, 4, 6 and 12 months of age. Infants younger than 6 months (too young to have completed the vaccine series), those with cochlear implants and children with certain immune problems are at greatest risk for pneumococcal infection.

"Parents who have chosen not to vaccinate their children just don't realize how important it is to take advantage of medical resources. They don't realize how lucky they are to have this opportunity for protection against serious diseases. Vaccines are the greatest medical advancement of my generation. Simply put, they save lives."

ALYSSA HUTCHENS
H1N1 INFLUENZA / CONQUERING

Amy and Marcus Hutchens wish that more parents would take seriously the dangers to their children's health from contracting the "flu." When asked to describe how sick their daughter became with the flu, Amy shows a recent photo of Alyssa, battling for her life in the intensive care unit. It's a powerful image matched by Amy's words, "My daughter is barely recognizable in this photo and almost died from the flu. Believe me, one of the most important things you can do for your child is get them flu vaccine."

Alyssa was a healthy, active teenage girl when she began to complain of a sore throat, cough and fever. Marcus took Alyssa to their local doctor, who diagnosed her with influenza A. Two days later, her fever spiked above 105, a rash appeared all over her body, and she said she couldn't feel her legs very well. Now feeling alarmed, Marcus took Alyssa back to their doctor, who quickly put her in an ambulance to the local hospital emergency room. The ER doctors there recommended an immediate transfer via helicopter to Children's Mercy Adele Hall Campus. The last thing Alyssa would remember for the next three-week period was being introduced to her flight crew. She lost consciousness en route to Children's Mercy and her bodily systems began to fail. Alyssa was diagnosed with H1N1 influenza-associated pneumonia, complicated by group A streptococcal bloodstream infection. In the Intensive Care Unit, Alyssa was placed into a medically induced coma, her liver and kidneys failed, and she was placed on dialysis. She stayed in a coma, on a ventilator, for 23 days and was in the hospital for a total of 43 days as she struggled to recover from the complications of H1N1 flu. As part of her treatment, Alyssa received an experimental drug for influenza.

Amy still finds it hard to believe that Alyssa became so sick, so fast, and she admits to "lots of heartache over the missed moments along the way," as Alyssa's health began a dangerous decline. Amy's voice crumbles as she contrasts Alyssa's life before and after she contracted the flu. Before, Alyssa was an active girl, playing a different sport each season and enjoying all the activities of middle school. Now, several years after her illness, Alyssa continues to find her way back, both emotionally and physically, to a normal teenage life. When she left the hospital, she needed physical and occupational therapists to teach her to walk and write again.

It was hard for Amy and Marcus to see Alyssa struggle to regain her normal life's routines. Amy explains that although Alyssa got back in school the year after her

illness, her spirits frequently sagged as she worked daily on rehab exercises at her local community center, and one day a week with a physical therapist, to regain her lost muscle and skeletal function and skills. She had surgery to repair one knee 14 months after leaving the hospital. Her pulmonary function remains weakened and her immune system is compromised. Since contracting H1N1, she is frequently sick and is highly susceptible to strep, stomach flu and/or other viral infections.

While everyone knows about influenza, many feel that it is a routine illness and it is not to be feared. Yet serious and fatal cases occur every year in the U.S. While there are antiviral drugs to treat influenza (e.g. Tamiflu®), they must be started in the first 24-48 hours of illness to have a chance to be effective. Traditionally infants and the elderly have been affected most seriously by influenza outbreaks each season. So infants and the elderly were initially the groups targeted for routine yearly influenza vaccine. Then the H1N1 pandemic influenza arose in 2009. It caused as much or more of the serious versions/deaths from "flu" in healthy teenagers and young adults as it did in infants and the elderly. It is now clear that everyone regardless of age is at some risk for serious influenza infection. That is the reason for the recent recommendation that all people who do not have a specific medical contraindication should receive influenza vaccine each year. There are two versions of influenza vaccine. There is the traditional "flu shot" and then there is also the nasal spray influenza vaccine. Side effects of the vaccines are usually mild lasting less than 48 hours. While no vaccine is 100 percent effective, for most of us influenza vaccines are expected to provide at least a 50 percent less chance that we get clinical disease due to influenza.

Amy says, "This near-death experience has been very hard for our family to recover from. I don't know that most people understand what it's like to almost lose a child. You never think you'll be in this situation. Words can't describe what it's like to see your child in a hospital bed, unrecognizable to you, unable to communicate with you, because they are so sick."

She encourages parents to slow down, double check their health care decisions and carefully consider what risks they choose to live with.

"You never think you'll be in this situation. Words can't describe what it's like to see your child in a hospital bed, unrecognizable to you, unable to communicate with you, because they are so sick."

BRANDON JERNIGAN
VARICELLA (CHICKENPOX) / CONQUERING

Brandon Jernigan was just shy of his fourth birthday when he was diagnosed with ALL, acute lymphoblastic leukemia, a cancer of the white blood cells. However, it was a case of chickenpox, or varicella, that potentially threatened his life and landed him the hospital just when his leukemia was becoming under control.

Brandon's parents, Alex and Cheryl, were shocked by his leukemia diagnosis and terribly concerned for their son's health. Brandon began receiving cancer treatments in the Children's Mercy Division of Hematology, Oncology and Bone Marrow Transplantation almost immediately. Initially, he stayed in the hospital for four days for further testing and consultations, and to begin his chemotherapy regimen.

For Brandon, life became a new routine involving dozens of trips to and from the hospital clinic for treatments and tests. Cheryl remembers the Children's Mercy nurses and doctors working with her as a team to ease any discomfort the treatments might cause her son. After a couple of months, Cheryl began to feel cautiously optimistic, considering it "lucky" that Brandon wasn't suffering from many of the debilitating side effects that can accompany chemotherapy treatments.

Five months into his treatments, Brandon received a cancer chemotherapy treatment known as delayed intensification. Following this treatment, he developed a blistering rash, lethargy and fevers. He was hospitalized and a diagnosis of chickenpox, varicella, was confirmed. The tests also showed that his chickenpox skin lesions were infected with group A streptococcus. This type of bacteria is a common cause of skin infections in healthy children, but can become life-threatening if it makes its way to the bloodstream.

With an immune system already compromised and weakened from his chemotherapy regimen, Brandon was hit hard by the chickenpox virus. In fact, Cheryl describes his chickenpox experience as being far worse than any of the side effects from his cancer drugs. Brandon received antibiotics for this "strep" infection and another medicine that is active against the chickenpox virus. He stayed in the hospital for nine days – five days longer than his initial stay for cancer treatments.

Like many parents, Alex and Cheryl still wonder where their son caught the chickenpox. Brandon had his first varicella shot when he was a 1-year-old. However, when children are actively being treated for cancer, they may not receive the same degree of effective protection from their immunizations.

The chickenpox virus was known to be circulating in Brandon's older brother's school at the time he was diagnosed with the virus, and so-called "breakthrough varicella" outbreaks were being seen across the country. These were light cases of the chickenpox disease present in children who had already been vaccinated before they were 3 years old. One year after Brandon's hospitalization, new recommendations emerged supporting the need for a second dose of the varicella vaccine for children prior to starting kindergarten.

The varicella vaccine program has eliminated 90 percent of deaths from the chickenpox disease. Before the varicella vaccine became available in 1995, virtually every child in the United States developed chickenpox. Hundreds of thousands of children developed the disease as the virus passed easily from person to person. While in most otherwise healthy children, chickenpox ran its course without complications, the

disease could rapidly progress in children with leukemia or other forms of immune deficiency, posing a potentially fatal threat.

However, there are still communities in which families and individuals refuse vaccination, so disease activity remains. Chickenpox remains a serious threat to children fighting cancer or other immune suppression diseases, and it can also be dangerous to otherwise healthy children.

After receiving cancer treatments for over three years, Brandon is now cancer-free. He has no lingering side effects from either the cancer treatments or the chickenpox. Fortunately, he has only vague memories of his days in the hospital and his many visits to clinics.

Today Brandon is an active, happy 9-year-old boy with a calm gaze and a sweet smile. He enjoys all the activities of a regular childhood, from school to outdoor fun to adventures with his older brother, Devin. Cheryl reflects, "We were blessed to be so close to Children's Mercy and to receive such great care."

Varicella (Chickenpox)

In the past, most parents and even many pediatricians regarded chickenpox as a benign, inevitable infection of childhood — with over 4 million cases occurring every year. Heralded by fever and the development of a typical itchy rash with blisters, the disease ran a course of five to seven days, sometimes leaving behind small scars from the skin lesions. If one child in a family developed chickenpox, 90 percent of the other susceptibles would develop chickenpox within 10-21 days. The chickenpox virus infects the sensory nerves without causing any damage and travels to the sensory ganglia where it becomes dormant (or latent) and remains for years. In older adults and in those whose immune system is impaired, the virus may reactivate causing the disease we call shingles.

While most children will recover from chickenpox uneventfully, before the implementation of chickenpox vaccine, 1,000 children were hospitalized with chickenpox each year and approximately 100 died annually from complications of their infection. Complications in healthy children were not uncommonly seen and manifest as bacterial infections of the skin, usually caused by either Staphylococcus aureus or group A streptococcus.

In the late 1980s and early 1990s, an increase in chickenpox complications related to group A streptococcus bacteria was noted in otherwise healthy children. In some of these children, the infection rapidly dissected through skin, fascia and muscle causing devastating infection that sometimes led to limb amputation. The media coined the term "flesh eating bacteria" and outbreaks of such infections often related to chickenpox infection were reported across the United States.

Varicella vaccine was introduced in 1995 for healthy children over 12 months of age and was widely implemented by the year 2000. A second dose of vaccine was recommended in 2006 and is now routinely given in children at 4-6 years of age. It is estimated that 95 percent of children are protected against severe varicella infection by virtue of vaccination, and overall, a decrease of 99.8 percent of varicella cases has been noted as of 2010.

Mild cases of varicella may still occur in otherwise healthy children and the virus can be passed on to others who are unimmunized, incompletely immunized, have a disease for which high-dose steroids are given, or have blood cancers or an immune deficiency. In a child whose immune system is impaired by cancer or an immune deficiency condition or who requires treatment with certain medications that suppress the immune system, the virus can spread to the lung, liver and/or brain, causing devastating organ dysfunction, and in some, death. Vaccine protection of all children is the goal — and underscores the importance of ensuring that herd immunity protects those who cannot receive vaccine.

TIM McQUAID
POLIO / NOT CONQUERED

Tim McQuaid contracted polio in 1953 when he was 3 months old as the disease swept through Kansas City. Destroying the muscles and connective tissues in his left leg, the disease forever changed the mechanics of his left knee and restricted his mobility. Tim was born on the edge of history, just months short of the medical breakthrough — the polio vaccine — that changed the country. This cruel disease would influence his childhood and mold his character, but Tim would not allow it to define him or his life's journey.

Tim's mother, Faith, a nurse and busy mother of six children, had followed the recommended precautions for preventing the spread of polio. As Tim grew up, and for years afterward, she wondered what she might have done differently to prevent the disease from seriously harming one of her children. But polio was an unpredictable disease, impacting some individuals more than others in a seemingly random fashion. Her first two children contracted the disease as infants in Minnesota, but suffered no lasting physical consequences. Tim's younger brother, John, born just 11 months after him as the polio vaccine was gaining traction, received the vaccine and was spared the disease.

As a young child, Tim hated it when people stared at him as he walked, but his parents said to pay them no mind. He was fitted with corrective shoes but often refused to wear them, insisting instead on normal shoes like the ones his siblings wore. His father, Sam, worked with him to try and improve his leg mobility, doing exercises to increase lateral movement. In hindsight, Tim laughs and asks, "How can you strengthen what's not there?" His weakened leg muscles never were able to produce the normal range of motion or strength for his left leg.

Tim believes now that his siblings and friends, a tight-knit group, must have felt more than a little pity for him in his early years, though he doesn't recall being aware of it at the time. He remembers his friends sticking up for him when he let his mouth run or waded into a fight he couldn't win. Unable and uninterested in playing sports, Tim discovered a lifelong passion and curiosity for machinery and how things work. As a teenager, he focused on lawnmowers, electronics and cars, and the child who wasn't supposed to walk became the young man who owned and operated his own lawn-mowing business

Today, Tim is a happily married man with his own construction business. He has a rolling gait and credits his parents' efforts for his physical mobility and for the philosophical resilience that has served him well throughout his life. His mother insisted he learn to walk without the recommended leg brace for his left leg because she hoped to promote his independence as an adult. His parents tried to treat their children equally, seeking to minimize the disruption of the disease on Tim's life; they focused instead on encouraging him to work through challenges to reach his personal goals.

With a hardy, determined mindset, every day Tim battles the consequences of his body's structural (skeletal) imbalance, which often takes its toll on his overall physical health. In

his self-deprecating way, Tim says he frequently falls down, as the structural weakness of his left side often causes him to lose balance. Over the years, he has broken an arm and a wrist, sprained his ankles, broken his good leg (the right femur), shattered his kneecap and twice broken his weaker left leg. He constantly scans the floor as he walks, appropriately cautious, knowing that the turned-up corner of a rug or any misstep could lead to another serious fall.

Tim says he looks for stair rails as he goes through his day, an apt metaphor for his outlook on life, and adds that life is full of risk. Why, he asks, would anyone go through life without taking advantage of the available protections?

Tim was born on the edge of history, just months short of the medical breakthrough that changed the country, the polio vaccine.

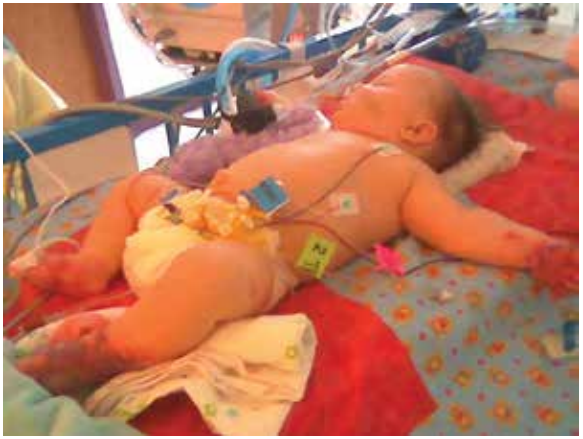
Most of us these days take for granted that polio is not in our communities. And that is true for most of the world. But polio is just a plane ride away. War and poverty have prevented some parts of the world like Pakistan from eradicating polio. Ongoing turmoil can provide a haven for polio. This is a disease that should never paralyze another child in the United States. Polio vaccine is highly effective. Side effects from the current killed vaccine, which comes as a shot, are minimal. Infants get the two doses in the first six months of life and children get boosters in the second and fourth-fifth year of life. This simple regimen has eradicated polio from our midst. The only way it would start up again is if people fail to immunize their children. Then if a case was imported from a place like Pakistan, for example, where cases were reported in 2015, polio would find children without vaccine protection, and they would be vulnerable to paralytic disease.

Tim believes in vaccination programs to prevent diseases. He supports the science and rational thought used by the medical community to better understand the complexity of the body and to help discover ways to protect from diseases that compromise lives.

ANNABELLE SPENCE
STREPTOCOCCUS PNEUMONIAE / NEARLY CONQUERED

When Elizabeth and Thomas Spence brought home their healthy, full-term baby daughter, Annabelle, they were delighted. Several weeks after her birth, Annabelle received her first vaccinations, and the family's pediatrician reassured the Spences that her development was right on track.

About six weeks later, Elizabeth became concerned when Annabelle started showing flu-like symptoms and took her to their pediatrician. She remembers being asked about Annabelle's vaccination record and double-checking her own records to verify that the baby had indeed received all of the recommended shots. The doctor examined Annabelle, and precautionary blood tests indicated a slightly low white blood cell count but otherwise normal results.



That evening, Annabelle's condition continued to deteriorate. She became more listless, and her parents – the experienced parents of two older children – were increasingly concerned. Early the next morning, Annabelle's pediatricians were alarmed by the significant, downward trend in her condition and recommended her immediate transfer via helicopter to Children's Mercy Adele Hall Campus. The Children's Mercy team admitted Annabelle to the Pediatric Intensive Care Unit (PICU) and diagnosed her as having meningitis and a bloodstream infection caused by Streptococcus pneumoniae. Elizabeth and Thomas were horrified to see their 10-week-old daughter immediately placed on full life support. In less than 72 hours, she had transformed from a happy, healthy baby to a child fighting for her life.

In the PICU, Annabelle's left side extremities were significantly impacted and Elizabeth recalls, "Her skin looked like she had third-degree burns." For a couple of days, the physicians considered the possibility of amputating her fingers, hand, arm or leg. They feared that the lack of blood supply to her left side extremities, a complication of the septic shock her body was experiencing, might necessitate this drastic procedure. They also worried that Annabelle might lose part or all of her hearing. For the Spences, this was a terrifying time, every day an emotional roller coaster, and the outcome was unpredictable.

Annabelle continued fighting for her life in the PICU for about a week before improving enough to move into a regular hospital room; she stayed at Children's Mercy for an additional two weeks before being well enough to return home.

Today, Annabelle is a smart, independent and inquisitive girl who has no memories of her time in the hospital. She looks at photos from that time and asks her parents, "Is that really me?" However, she does have physical reminders of the disease. The skin on parts of her left side remains

slightly scarred and her left foot is swollen when compared to her right one. She is unable to wear cutesy girl shoes and prefers the sturdier soles of a more supportive shoe.

When reflecting today on this scary chapter in her daughter's life, Elizabeth feels grateful that she trusted her instincts and took Annabelle to the doctor as soon as she sensed that something wasn't right.

Certain children are at higher risk for this type of infection. In Annabelle's case, she was born without a spleen and remains susceptible to infections throughout her life. But she is the exception to the rule. Almost all children contracting this type of infection are completely healthy, emphasizing the importance of this vaccine and the need to get infants immunized on schedule.

Before routine use of a vaccine that became available in 2000, *Streptococcus pneumoniae* was the most common cause of bloodstream infections in children.

Streptococcus Pneumoniae Infections

Streptococcus pneumoniae (also called pneumococcus) is one of the most common bacteria causing the majority of serious ear infections in children. While ear infections are usually easily identified and treated with antibiotics, some children have recurrent episodes of ear infection and may suffer hearing loss and/or require surgery to place ear tubes.

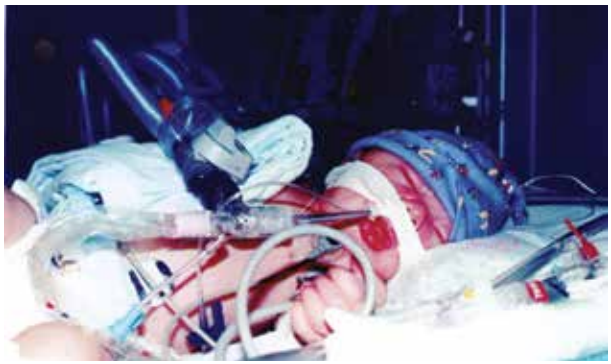
Long recognized as a part of the normal flora in the nasopharynx of many children, if the bacteria makes its way into the bloodstream, it can disseminate to other organs causing infection in the lungs (pneumonia), brain (meningitis), bone (osteomyelitis), joint (septic arthritis) or heart (pericarditis and endocarditis).

The Antibiotic-Resistant Era

Prior to the 1980s, there were just a few of the over 90 serotypes of pneumococcus that were the most frequently implicated in pediatric infections — and for the most part, such infections were easily treated with penicillin or amoxicillin. By the early to mid 1990s, the bacteria had become resistant to many antibiotics, and treatment of the most serious infections became increasingly challenging. Vaccines were developed to target those serotypes associated with antibiotic resistance and the first generation conjugate vaccines were licensed and implemented in the year 2000. A major reduction in pneumococcal infection was seen but increasingly, new serotypes emerged. In 2010, the second-generation vaccine which now covered 13 of the most frequently identified serotypes was implemented.

CHRISTOPHER FARRELL
PERTUSSIS / NEARLY CONQUERED

Fifteen years ago, the last patient Kathleen Farrell, MD, saw in private practice at 4 p.m., before starting maternity leave in September 1999, was an 11-year-old boy with an unusual cough and hip pain. Now on staff at Children's Mercy Kansas City, at the time Dr. Farrell was in a private practice in Orlando, Fla. While evaluating her patient's hip, she noticed a cough that was taking his breath away and producing a whooping sound, and suspected the diagnosis of whooping cough (pertussis), especially since the boy had never completed the DTP series.



Following that appointment, Dr. Farrell developed a cough and was given treatment with an antibiotic that did not treat pertussis. After completing a 10-day course of antibiotics, she was no better and her cough progressed to an intensity that brought on early labor.

Dr. Farrell gave birth to her son, Christopher, just shy of 37 weeks. Christopher developed a cough 20 days after birth. Dr. Farrell consulted the partners in her pediatrics practice about treating him for pertussis, given her exposure and symptoms at the time of delivery. Instead, Christopher was given several other diagnoses including gastroesophageal reflux. One of her colleagues agreed that Chris's color didn't look right after feeding, and when he began projectile vomiting, she and another pediatrician tested Christopher for Bordetella pertussis.

Christopher developed additional symptoms and was immediately rushed to Arnold Palmer Hospital for Children in Orlando, Fla., where he was admitted to the Pediatric Intensive Care Unit (PICU) after he had an episode where he stopped breathing. He was evaluated for sepsis and several specialists were consulted, including gastroenterology, pulmonary and cardiology, and the intensivist. The gastroenterologist and pulmonologist thought Christopher had gastroesophageal reflux. Cardiology diagnosed him with an innocent heart murmur. The pediatric intensivist shared Dr. Farrell's conviction that Christopher had pertussis.

Test results confirmed that Christopher indeed had Bordetella pertussis and it had advanced to stage 3. There are three stages to pertussis and infants who develop pertussis at less than 6 months of age are most at risk for serious complications and death. The first stage of pertussis is similar to a cold (called the "catarrhal" stage) and lasts two weeks. The second stage is marked by a cough that occurs in spells (paroxysms of cough) and coughing spells are commonly followed by vomiting. The classic inspiratory whoop may be heard in older children, but is less common in young infants. The third stage, "paroxysmal" stage of whooping cough, lasts eight to 10 weeks, followed by a convalescent or recovery period where the cough lessens over time. Children often require three months to recover fully from whooping cough. Sudden unexpected death can be caused by pertussis. The disease is particularly severe in preterm and unimmunized patients.

The Farrell family's ordeal continued for 100 days, including two weeks in the PICU, three weeks on a ventilator, intubation and extubation four times until he was stable

There has been a large resurgence of pertussis. It is important that all babies receive the primary series of vaccinations at 2 months, 4 months and 6 months so they are protected. It is now recommended that every pregnant woman receive Tdap with every pregnancy.

without the ventilator. It was, in Dr. Farrell's words, "the most trying and difficult time in my life. We were so afraid Christopher wouldn't survive. "

Christopher is now a healthy, active 15-year-old. He's an excellent student who enjoys the drums and playing sports. He is a fighter and lucky to have survived this ordeal.

"Fifteen years ago, I don't believe most physicians saw pertussis as a threat to our patients," Dr. Farrell says. Since that time, there has been a large resurgence of pertussis. It is important that all babies receive the primary series of vaccinations at 2 months, 4 months and 6 months so they are protected. Booster doses should be given at 15 months, 5 years and 11 years. It is now recommended that every pregnant woman receive Tdap with every pregnancy – in either the second or third trimester. This is currently the most effective way to protect the youngest infants who are too young for vaccine and most at risk for severe complications.

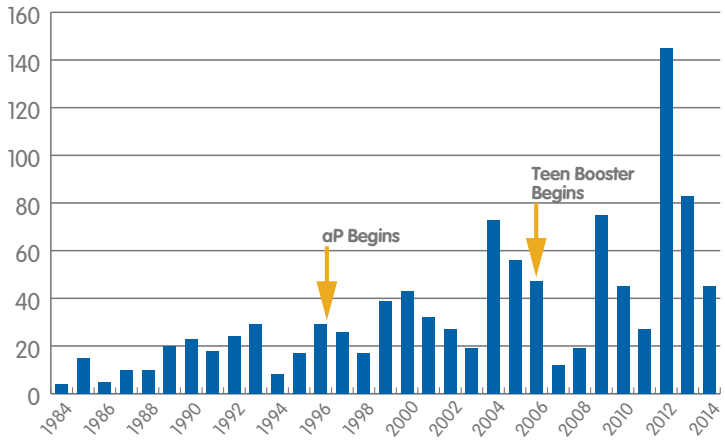
"Being in the PICU was very challenging, and I remember aching to hold my son," Dr. Farrell says. Christopher's 100-day ordeal could have been prevented. Pertussis is real and life-threatening. Particularly vulnerable are those like Christopher who are too young to receive the vaccine.

In the last 10 years, doctors at Children's Mercy Kansas City diagnose an infant or child with whooping cough on a weekly basis. The increase in disease now compared to 30 years ago is related to several factors. The first vaccine introduced to protect against pertussis was very effective, but in some patients caused high fevers and was replaced by a new vaccine in the mid 1990s. The newer so-called "acellular" pertussis vaccine is very safe but less protective than the old "whole-cell" vaccine.

Importantly, more parents are foregoing immunizations or delaying vaccines in their children. This places their child and other children at risk. Pertussis spreads easily and nearly 90 percent of those exposed who are susceptible to pertussis will develop disease.

Researchers are working on improving the current vaccine and tracking changes in the bacteria itself. Still, routine immunization remains the most important strategy to protect babies and children from whooping cough — and vaccination for babies and children and for mothers during pregnancy are the top priorities.

Bordetella pertussis Children's Mercy 1984-2014
31 years experience



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Christopher J. Harrison, MD

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Dr. Harrison received a bachelor's degree, medical degree and performed his pediatric residency training at the University of Kentucky in Lexington plus pediatric infectious diseases training at the University of Oklahoma in Oklahoma City. He served as faculty at Cincinnati Children's Hospital Medical Center, Creighton University Medical School, and University of Louisville School of Medicine prior to becoming Professor of Pediatrics at Children's Mercy Kansas City, Pediatric Infectious Diseases Section, in Kansas City, Missouri, and the University of Missouri-Kansas City. He is director of the Children's Mercy Infectious Diseases Research laboratory, co-principal investigator on the Kansas City site for the CDC-sponsored New Vaccine Surveillance Network (NVSN), Director of the Kansas City site for the NIH-sponsored pediatric Vaccine and Treatment Evaluation Unit (VTEU).

Dr. Harrison is a fellow of the American Academy of Pediatrics, Pediatric Infectious Disease Society (PIDS) and Infectious Disease Society of America (IDSA). He is a member of the Society for Pediatric Research, American Pediatric Society and American Society for Microbiology. He serves on the PIDS Clinical Affairs Committee, the Vaccine Advocacy Committee and PIDS Publications Committee. He is on the ABP writing group for ID Sub-Boards and also for the 2016 IDSA/PIDS Bone and Joint infection Guidelines.

Board certified in pediatrics and pediatric infectious disease, Dr. Harrison's clinical and research interests include the development/efficacy of vaccines, pharmacokinetics, antimicrobial resistance, innate immunity to cytomegalovirus, human parechovirus, and management of bacterial respiratory and bone/joint infections.

RESOURCES

1. Parent's Guide to Childhood Immunization www.cdc.gov/vaccines

2. American Academy of Pediatrics Immunization Initiative www.aap.org/immunization

3. Vaccine Education Center at Children's Hospital of Philadelphia http://vaccine.chop.edu

4. Provider Resources for Vaccine Conversations with Parents www.cdc.gov/vaccines/hcp/patient-ed/conversations/

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